REMARKS

Claims 26-72 were pending. Applicants herein canceled claim 72 without prejudice. In addition, applicants amended claims 26, 30, 33, 61 and 71. This amendment does not involve any issue of new matter. Support may be found inter alia in the specification on page 6, lines 22-25. Accordingly, entry is respectfully requested such that claims 26-71 will be pending.

Rejection under 35 USC §112, second paragraph

The Office Action rejected claims 58 and 72 under 35 USC §112, second paragraph as allegedly being indefinite. The Office Action states that claim 72 recites a use without setting forth any steps involved in the process. In response, applicants without conceding the correctness of the Examiner's position but to expedite prosecution of the subject application have herein canceled claim 72 without prejudice to their right to pursue the subject matter of this claim at a later date either in this or another application.

In addition, the Office Action states that in claim 58, the term "small" is a relative term which renders the claim indefinite. In response, applicants respectfully traverse. Applicants submit that terms such as "small molecule" and "small organic compound" are terms of art whose meaning are understandable by those skilled in the art. A review of the literature prior to the priority date, *i.e.* December 29, 2000 reveals that it was well accepted that small molecules are compounds with a molecular weight of less than 1000 daltons. In support, applicants respectfully direct the Examiner's attention to the following exemplary citations:

> (1) Free Radical Toxicology (Target Organ Toxicology Series) by Kendall B. Wallace, Publisher: Taylor & Francis; (June 1997), ISBN: 1560326328, which states on page 148 "... is associated with three chemically distinct types of oxidants formed by iron-mediated Fenton reactions in the presence of DNA. Small-Molecule Antioxidants Numerous **small molecules (<1000 MW)** with high reactivity toward oxidants have been described. Three of these, vitamin E, ascorbic acid, and glutathione, play essential ..." [emphasis added];
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> (2) Molecular Methods for Virus Detection by Danny Wiedbrauk and Daniel Farkas, Publisher: Academic Press, 1st edition (January 1 5, 1995), ISBN: 0127489207, which

states on page 154 "Electrochemiluminescent labels are relatively **small molecules (--1000 dalton)** that are extremely stable and may be coupled to nucleic acids, hap- tens, or proteins without affecting immunoreactivity or ..."; [emphasis added]

(3) Neurotoxicology: In Vitro by V. W. Pentreath (Editor), Publisher: Taylor & Francis; 1 edition (June 1, 1999), ISBN: 0748403884, which states on page 200 "... Modalities of intercellular communication. Hormones (V) and growth factors (0) are transported to the targets via blood. Ions and **small molecules (< 1000 Da)** can pass through gap junctions from one cell to its neighbours and influence the function of the connecting cells. ..." [emphasis added]

(4) New Frontiers in Cancer Causation: Proceedings of the Second International Conference on Theories of Carcinogenesis, by Olav Hilmar Iversen (Editor), Publisher: Taylor & Francis, (September 1993), ISBN: 1560322519, which states on page 186 "... (connexons). Each cell contributes a hemichannel composed of a hexamer of proteins (connexins). Clusters of these connexons allow ions and **small molecules (below 1000 daltons)** to freely equilibrate between coupled cells. There exists a family of highly conserved genes coding for these proteins ..." [emphasis added]

(5) Pesticide Residues in Foods : Methods, Techniques, and Regulations, by W. George Fong, H. Anson Moye, James N. Seiber, John P. Toth, Publisher: Wiley-Interscience; (January 22, 1999), ISBN: 0471574007, which states on page 217 "... lymphocytes and others. Such an immunoglobin is called an antibody, and is the molecular basis on which immuoassays are built. **Small molecules (less than - 1000 daltons)**, called haptens, seldom produce such a response, and are not immunogenic, but become so when covalently bonded to a ..." [emphasis added]

(6) Dermatotoxicology by Francis Nicholas Marzulli (Editor), Howard I. Maibach (Editor), Publisher: Taylor & Francis; 5th edition (February 1996), ISBN: 1560323566, which states on Page 147 "... with skin proteins to form complete antigens and how these structures are recognized by T-cell receptors. SOME CHEMICAL REMINDERS Haptens (**small molecules with a molecular mass less than 1000 Da**) interact with

biological macromolecules by mechanisms leading to the formation of bonds of various strengths between the two entities. ..." [emphasis added]

Accordingly, applicants submit that the above citations shows the well accepted meaning of small molecules or small organic compounds, and that the meaning of such terms would be understood by one skilled in the art. In re Hammack, 166 USPQ 204, 208 (C.C.P.A 1970). Accordingly, applicants respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Rejection under 35 USC §102 - claims 26-56 and 58-72

The Office Action rejected claims 26-56 and 58-72 under 35 USC §102(b) as being allegedly anticipated by Tracy et al. In response, applicants respectfully traverse. Nevertheless, applicants without conceding the correctness of the Examiner's position but to expedite prosecution of the subject application have herein amended the claims. For example, amended claim 26 recites as follows: [a] sustained release formulation comprising one or more biologically active molecules prepared by exposure of the biologically active molecules in aqueous solution to an organic solvent **resulting in** a precipitate, lyophilate or crystal. [emphasis added].

Applicants would like to highlight two points of distinction of applicants' claimed invention from Tracy. First, Tracy et al. states that the IFN is in a polymer solution which is dispersed into droplets which are then *"frozen by means suitable to form microparticles." See* column 7, lines 5-6. For instance, liquified gas *(see* column 7, lines 11-13) or supercooled liquid (*see* column 7, lines 18-20) can be used to form microparticles by freezing the droplets of IFN-polymer solution Accordingly, in Tracy, the polymer microparticles are formed *by freezing, not by precipitation,* prior to any exposure to the frozen nonsolvent ethanol; preformed microparticles simply "sink to the surface of the nonsolvent" ethanol. *See* column 7, lines 5-14. Thus, in Tracy, the controlled release particle compositions are formed by a process of freezing rather than by any precipitation process. In contrast, in applicant's invention, an organic solvent results in the precipitation. Second, Tracy releases the IFN from a required "polymeric matrix." *See e.g.* column 1, lines 40-41 and 48-49 and column 2, lines 26-29. Applicants do not use any such polymeric matrix in their invention. Accordingly, applicants contend that these amendments and remarks obviate the Examiner's rejection and respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Rejection under 35 USC §102 - claims 26-56 and 58-59 and 67-72

The Office Action rejected claims 26-56 and 58-72 under 35 USC §102(b) as being allegedly anticipated by Violanto et al. In response, applicants respectfully traverse. Nevertheless, applicants without conceding the correctness of the Examiner's position but to expedite prosecution of the subject application have herein amended the claims. Again, applicants point out that amended claim 26 recites as follows: [a] sustained release formulation comprising one or more biologically active molecules prepared by exposure of the biologically active molecules **in aqueous solution** to an organic solvent **resulting in** a precipitate, lyophilate or crystal. [emphasis added].

Applicants would like to highlight two points of distinction between applicants' claimed invention and the invention disclosed in Violanto. First, Violanto's method begins by dissolving a solid organic compound in an organic solvent. *See* column 2, lines 63-65. Violanto states that the organic solvent in which the solid organic compound is dissolved can be DMSO, DMF, NNDMA, phenol, isopropanol, or other solvents. *See* column 3 lines 49-51. These are clearly organic solvents, and not aqueous. Furthermore, Violanto states that the compound has "essentially little aqueous solubility." *See* column 2, lines 65-66. In contrast, applicant's claimed method begins with the compound in aqueous solution, not in an organic solvent.

Second, Violanto uses an "aqueous precipitating liquid" in order to precipitate an organic compound out of organic solution. *See* column 2, lines 66-67. In contrast, in applicants claimed invention, the organic solvent results in the precipitation of the compound from aqueous solution. Thus, whereas in Violanto, the organic solvent solubilizes the solid, in applicant's claimed invention, the organic solvent precipitates the compound. Applicants contend that these amendments and remarks obviate the Examiner's rejection and respectfully request that the Examiner reconsider and withdraw this ground of rejection.

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to pass this application to issue.

Applicant believes no fee is due with this response. However, if a fee is due, please charge our Deposit Account No. 18-1945, under Order No. PBLI-P01-010 from which the undersigned is authorized to draw.

Dated: March 15, 2004

Respectfully submitted,

By_____

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